EUROPEAN COMMISSION
DIRECTORATE-GENERAL FOR HEALTH AND FOOD SAFETY

The Director General

Brussels,
SANTE/E5/CS/mcd 379717

Sent by e-mail only

Dear Prof Rasi,

Subject: Implementing measures under Article 77(6) of Regulation (EU) 2019/6 on veterinary medicinal products[1] regarding good pharmacovigilance practice

On 7th January 2019, the new Regulation on veterinary medicinal products ('VMP Regulation') was published.

In accordance with its Article 160, it will start applying 3 years from its entry into force, i.e. from 28th January 2022.

According to Article 77(6), the Commission shall adopt an implementing act to establish measures on good pharmacovigilance practice. This implementing act should be adopted by the date of application of the VMP Regulation.

In this context, I would like to ask you to provide us with the Agency's scientific recommendations on good pharmacovigilance practice, by taking into account the following:

[1] Regulation (EU) 2019/6 of the European Parliament and of the Council of 11 December 2018 on veterinary medicinal products and repealing Directive 2001/82/EC, OJ L 4, 7.1.2019, p. 43.

Prof Guido Rasi
Executive Director
European Medicines Agency
30 Churchill Place
Canary Wharf
London E14 5EU
United Kingdom

- the experience gained with the application of the current system as established in VOLUME 9B of The Rules Governing Medicinal Products in the European Union – Guidelines on Pharmacovigilance for Medicinal Products for Veterinary Use –.
- the signal management process defined in Article 4, provided for in Article 81 and outlined in Recital 63 of the VMP Regulation.
- the experience gained with human signal management process as laid down in Commission Implementing Regulation (EU) No 520/2012 and the Guidelines on good pharmacovigilance practices (GVP) .
- the responsibilities of marketing authorisation holders as referred to in Articles 58 and 77 and his qualified person responsible for pharmacovigilance as well as rules for communication.
- the responsibilities of competent authorities as referred to in Articles 79 and 81(3-6) as well as rules for communication.
- reporting and recording of suspected adverse events as referred to in Article 76 as the necessary requirements for a smooth working of the pharmacovigilance data base and an effective signal management process.
- Calculation of incidence of suspected adverse events given in the database according to Article 75(3).
- the specific rules on pharmacovigilance inspections referred to Article 126.

Relevant excerpts from the VMP Regulation are included in Annex I for your convenience.

We would kindly ask for your contribution by the end of May 2020. This act is included in the first package for implementation in order to allow, on an exceptional basis, for an extended period for scientific advice. In these circumstances, we request a brief interim report by end of September 2019.

We would like to thank you for your collaboration.

Yours sincerely,

Anne Bucher

Encl. : Annex I

Annex I

Relevant excerpts from the VMP Regulation.

Recital 58

In the light of experience, it has become clear that it is necessary to take measures to improve the operation of the pharmacovigilance system. That system should integrate and monitor data at Union level. It is in the interest of the Union to ensure that the veterinary pharmacovigilance systems for all authorised veterinary medicinal products are consistent. At the same time, it is necessary to take account of changes arising as a result of international harmonisation of definitions, terminology and technological developments in the field of pharmacovigilance.

Recital 63

The procedures that competent authorities and the Agency will adopt in order to evaluate the information on suspected adverse events that they receive should comply with the measures on good pharmacovigilance practice which should be adopted by the Commission and, as appropriate, be based on a common standard derived from the current Commission guidelines on pharmacovigilance for veterinary medicinal products. The evaluation performed by the competent authority or the Agency in that way may be one of the means by which it is determined whether there is any change to the benefit-risk balance of those veterinary medicinal products. It is, however, emphasised that the signal management process is the 'gold standard' for that purpose and proper attention should be given to it. That signal management process consists of tasks of signal detection, validation, confirmation, analysis and prioritisation, assessment and recommendation for action.

Article 4

Definitions

For the purposes of this Regulation, the following definitions apply: (…)

(30) 'pharmacovigilance' means the science and activities relating to the detection, assessment, understanding and prevention of suspected adverse events or any other problem related to a medicinal product; (…)

(41) ‘signal management process’ means a process for performing active surveillance of pharmacovigilance data for veterinary medicinal products in order to assess the pharmacovigilance data and determine whether there is any change to the benefit-risk balance of those veterinary medicinal products, with a view to detecting risks to animal or public health or protection of the environment;

Article 58

Responsibilities of the marketing authorisation holders

(…)

10. The marketing authorisation holder shall without delay inform the competent authority which has granted the marketing authorisation or the Commission, as applicable, of any prohibition or restriction imposed by a competent authority or by an authority of a third country and of any other new information which might influence the assessment of the benefits and risks of the veterinary medicinal product concerned, including from the outcome of the signal management process carried out in accordance with Article 81. (…)

Article 74

Union pharmacovigilance database

1. The Agency shall, in collaboration with Member States, establish and maintain a Union pharmacovigilance database for the reporting and recording of suspected adverse events referred to in Article 73(2) (the "pharmacovigilance database"), which shall also include the information on qualified person responsible for pharmacovigilance as referred to in Article 77(8), the reference numbers of the pharmacovigilance system master file, the results and outcomes of the signal management process and results of pharmacovigilance inspections in accordance with Article 126.(…)

Article 75

Access to the pharmacovigilance database

(…)

3. The general public shall have access to the pharmacovigilance database, without the possibility to change the information therein, as regards the following information:

(a) the number and at the latest within two years from 28 January 2022 the incidence of suspected adverse events reported each year, broken down by veterinary medicinal product, animal species and type of suspected adverse event;

(b) the results and outcomes referred to in Article 81(1) that arise from the signal management process performed by the marketing authorisation holder for veterinary medicinal products or groups of veterinary medicinal products.

Article 76

Reporting and recording of suspected adverse events

1. Competent authorities shall record in the pharmacovigilance database all suspected adverse events which were reported to them and that occurred in the territory of their Member State, within 30 days of receipt of the suspected adverse event report.

2. Marketing authorisation holders shall record in the pharmacovigilance database all suspected adverse events which were reported to them and that occurred within the Union or in a third country or that have been published in the scientific literature with regard to their authorised veterinary medicinal products, without delay and no later than within 30 days of receipt of the suspected adverse event report.

3. The Agency may request the holder of a marketing authorisation for centrally authorised veterinary medicinal products, or for nationally authorised veterinary medicinal products in cases where they fall within the scope of a Union interest referral referred to in Article 82, to collect specific pharmacovigilance data additional to the data listed in Article 73(2) and to carry out post-marketing

surveillance studies. The Agency shall state in detail the reasons for the request, set an appropriate time limit and inform competent authorities thereof.

4. Competent authorities may request the holder of a marketing authorisation for nationally authorised veterinary medicinal products to collect specific pharmacovigilance data, additional to the data listed in Article 73(2) and to carry out post-marketing surveillance studies. The competent authority shall state in detail the reasons for the request, set an appropriate time limit and inform other competent authorities and the Agency thereof.

Article 77

Pharmacovigilance responsibilities of the marketing authorisation holder

(…)

5. The marketing authorisation holder shall comply with good pharmacovigilance practice for veterinary medicinal products.

6. The Commission shall, by means of implementing acts, adopt necessary measures on good pharmacovigilance practice for veterinary medicinal products and also on the format and content of the pharmacovigilance system master file and its summary. Those implementing acts shall be adopted in accordance with the examination procedure referred to in Article 145(2). (…)

Article 78

Qualified person responsible for pharmacovigilance

1. The qualified person responsible for pharmacovigilance as referred to in Article 77(8) shall ensure that the following tasks are carried out:

(a) elaborating and maintaining the pharmacovigilance system master file;

(b) allocating reference numbers to the pharmacovigilance system master file and communicating that reference number to the pharmacovigilance database for each product;

(c) notifying the competent authorities and the Agency, as applicable, of the place of operation;

(d) establishing and maintaining a system which ensures that all suspected adverse events which are brought to the attention of the marketing authorisation holder are collected and recorded in order to be accessible at least at one site in the Union;

(e) compiling the suspected adverse event reports referred to in Article 76(2), evaluating them, where necessary, and recording them in the pharmacovigilance database;

(f) ensuring that any request from the competent authorities or the Agency for the provision of additional information necessary for the evaluation of the benefit-risk balance of a veterinary medicinal product is answered fully and promptly;

(g) providing competent authorities or the Agency, as applicable, with any other information relevant to detecting a change to the benefit-risk balance of a veterinary medicinal product, including appropriate information on post-marketing surveillance studies;

(h) applying the signal management process referred to in Article 81 and ensuring that any arrangements for the fulfilment of responsibilities referred to in Article 77(4) are in place;

(i) monitoring the pharmacovigilance system and ensuring that if needed, an appropriate preventive or corrective action plan is prepared, implemented and, where necessary, ensuring changes to the pharmacovigilance system master file;

(j) ensuring that all personnel of the marketing authorisation holder involved in the performance of pharmacovigilance activities receives continued training;

(k) communicating any regulatory measure that is taken in a third country and is related to pharmacovigilance data to the competent authorities and to the Agency within 21 days of receipt of such information.

2. The qualified person referred to in Article 77(8) shall be the contact point for the marketing authorisation holder regarding pharmacovigilance inspections.

Article 81

Signal management process

1. Marketing authorisation holders shall carry out a signal management process for their veterinary medicinal products, if necessary, taking into account sales data and other relevant pharmacovigilance data of which they can reasonably be expected to be aware and which may be useful for that signal management process. That data may include scientific information gathered from scientific literature reviews.

2. Where the outcome of the signal management process identifies a change to the benefit-risk balance or a new risk, marketing authorisation holders shall notify it without delay and no later than within 30 days to the competent authorities or to the Agency, as applicable, and take the necessary action in accordance with Article 77(10).

   The marketing authorisation holder shall record, at least annually, all results and outcomes of the signal management process, including a conclusion on the benefit-risk balance, and, if applicable, references to relevant scientific literature in the pharmacovigilance database.

   In the case of veterinary medicinal products referred to in point (c) of Article 42(2), the marketing authorisation holder shall record in the pharmacovigilance database all results and outcomes of the signal management process, including a conclusion on the benefit-risk balance, and, if applicable, references to relevant scientific literature according to the frequency specified in the marketing authorisation.

3. The competent authorities and the Agency may decide to perform a targeted signal management process for a given veterinary medicinal product or a group of veterinary medicinal products.

4. For the purpose of paragraph 3, the Agency and the coordination group shall share the tasks related to the targeted signal management process and shall jointly select for each veterinary medicinal product or group of veterinary medicinal products a competent authority or the Agency as responsible for such targeted signal management process (‘lead authority’).

5. When selecting a lead authority, the Agency and the coordination group shall take into account the fair allocation of tasks and shall avoid duplication of work.

6. Where the competent authorities or the Commission, as applicable, consider that follow-up action is necessary, they shall take appropriate measures as referred to in Articles 129, 130 and 134.

Article 126

Specific rules on pharmacovigilance inspections

1. The competent authorities and the Agency shall ensure that all pharmacovigilance system master files in the Union are regularly checked and that the pharmacovigilance systems are being correctly applied.

2. The Agency shall coordinate and the competent authorities shall carry out inspections on the pharmacovigilance systems of veterinary medicinal products authorised in accordance with Article 44.

3. The competent authorities shall carry out inspections on the pharmacovigilance systems of veterinary medicinal products authorised in accordance with Articles 47, 49, 52 and 53.

4. The competent authorities of the Member States in which the pharmacovigilance system master files are located shall carry out inspections of the pharmacovigilance systems master files.

Article 145

Standing Committee on Veterinary Medicinal Products

1. The Commission shall be assisted by the Standing Committee on Veterinary Medicinal Products (‘the Standing Committee’). The Standing Committee shall be a committee within the meaning of Regulation (EU) No 182/2011.

2. Where reference is made to this paragraph, Article 5 of Regulation (EU) No 182/2011 shall apply.